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Correlation of Muscle Enzymes with Tsh In Hypothyroidism

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ABSTRACT:

Introduction*:** Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone or, more rarely, from their impaired activity at tissue level. This study was designed to estimate the muscle markers level in hypothyroidism cases and to assess the correlation with TSH. ***Methodology*:** Methods: In this study thyroid function tests (T3, T4 &TSH), serum muscle enzymes (CK, CKMB, LDH & AST) were measured in 100 newly diagnosed hypothyroid patients attending the Medical OPD and Laboratory of the Biochemistry Department of JLN Medical College & Hospitals, Ajmer. The results of patients were compared with 50 healthy controls of either sex of similar age group. The blood samples were collected from all the attending patients and analyzed for various serum muscle markers. ***Results*:-**A significant increased in the levels of CK-NAC, LDH and AST and non significant elevated level of CK-MB was observed in hypothyroid cases as compared to the healthy controls. A positive correlation was found between CK, CKMB, LDH & AST levels with TSH levels and negative correlation was found with T3 and T4 levels. ***Conclusion: The significant elevation of serum CK, LDH & AST activities indicate muscle involvement in hypothyroidism and that these enzymes can be used as parameters for screening of hypothyroid patients.

Keywords: Hypothyroidism, CK, CKMB, LDH, AST.

Introduction

Hypothyroidism, or underactive thyroid, develops when the thyroid gland fails to produce or secrete as much thyroxine (T4) as the body needs because T4 regulates such essential functions as heart rate, digestion, physical growth and mental development, an insufficient supply of this hormone slows life sustaining processes, damage organs and tissues in every part of the body, and can lead to life-threatening complications. Hypothyroidism can cause several symptoms, ranging from mild (e.g. fatigue, weight gain, cold intolerance, mental slowing, muscle cramping) to severe (e.g. heart enlargement, myxodema coma). Without regards to the cause of hypothyroidism, neuromuscular and musculoskeletal manifestations can be observed in many patients with the condition[1].

The patients with hypothyroidism do have myopathy rather than functional muscle disease. Serum CK was first used as a diagnostic aid in progressive muscular dystrophy[4].

It has since then become important clinical marker for muscle damage. The serum CK levels in healthy individuals depend on age, race, lean body mass and physical activity[2,3,4]. Musculoskeletal disorders often accompany thyroid dysfunction. In addition to well-known observation that musculoskeletal disorders are common in patients with hypothyroidism, they are also observed in thyrotoxicosis and level of CK is altered in both these conditions[5].

In recent years, studies have been conducted to establish a relationship of CK levels in thyroid diseases[6]. Skeletal muscle is affected by hypothyroidism more profoundly in cases of

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overt hypothyroidism and less so when subclinical hypothyroidism is present[7,8].

A majority of patients with hypothyroidism have been shown to have an increased serum CK. Furthermore only a few studies have investigated serum lactate dehydrogenase (LDH) and aspartate transaminase (AST) activity in patients with thyroid dysfunction. The present study was carried out to study muscle enzymes (creatine kinase, creatine kinase-MB, lactate dehydrogenase and aspartate aminotransferase) in cases of overt hypothyroidism and to correlate their levels with tri-iodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) levels.

Materials and Methods: The present study was conducted on 100 hypothyroid patients (Group II) attending the Medical OPD and Radio Immmuno Assay (RIA) Laboratory of the Biochemistry Department of JLN Medical College & Hospitals. Ajmer. The results of patients were compared with 50 healthy control (Group I) subjects of either sex of similar age group. Blood sarnples were collected by venipuncture by aseptic technique. The serum separated from the samples were analyzed for following biochemical parameters. Serum levels of T3, T4 and TSH were measured by RIA rnethod. The serrum rnuscle enzymes were estimated (by the NAC Kinetic UV method for Creatine kinase, by the immunoinhibition Kinetic UV rnethod for CK-MB, by the Pyruvate kinetic UV method for LDH, by the IFCC Method for AST after taking approval from ethical committee. SPSS. 13/win statistical software was used for analyzing the data. The results were expressed as mean ± standard deviation (SD). P-value < 0.05 was considered statistically significant.

***Results*:**

The present study had been concluded on 150 subjects with age group 25-55 years. These were further divided into 2 groups. Group I comparised of 50 subjects who were healthy controls and Group II comparised of 100 subjects who were hypothyroid patients.

Table 1: Comparison of biochemical parameters in both studied groups.

Sr. No.	Parameters	Healthy Controls (Mean ± S.D.)	Hypothyroid Patients (Mean ± S.D.)	p- value
1	Total T3 (ng/ml)	1.1 ± 0.3	0.43± 0.20	0.0001**
2	Total T4 (µg/dl)	7.59 ± 1.58	3.6 ± 1.4	0.0001**
3	TSH (µIU/ml)	2.79 ± 1.22	32.0 ± 12.1	0.0001**
4	CK-NAC (24-195 IU/L)	106.75±34.89	230.9±89.0	0.0001**
5	CK-MB(0-25 IU/L)	10.27±3.35	11.8±5.6	0.21NS
6	LDH (230-460 IU/L)	155.79 ±29.50	243.5±70.90	0.0001**
7	AST/SGOT(0-37 IU/L)	20.01±7.61	45.3±25.7	0.0001**

Note: $p > 0.05$ = Not significant (NS) ; * $p < 0.05$ = Significant; **$p < 0.001$ = Highly significant (HS).

Table 2: Pearson correlation of muscle enzymes with thyroid parameters.

Sr. No.	Muscle enzymes	T3	T4	TSH
1	CK-NAC	r = -0.51 P=0.009	r = -0.77 P=0.0001	r = +0.83 P=0.0001
2	CK-MB	r = -0.45 P=0.014	r = -0.68 P=0.0001	r = +0.73 P=0.0001
3	LDH	r =-0.41 P=0.027	r = -0.66 P=0.0001	r = +0.75 P=0.0001
4	AST/SGOT	r = -0.38 P=0.20	r = -0.65 P=0.0001	r = +0.67 P=0.0001

Note: p > 0.05 = Not significant (NS); * p < 0.05 = Significant; **p < 0.001 = Highly significant (HS).

Table 1 shows a highly significant increased in the levels of TSH, CK-NAC, LDH & AST and highly significant decreased in the levels of T3 & T4 and non significant elevated level of CK-MB was observed in hypothyroid patients as compared with healthy controls. This study also indicates that serum muscle enzymes correlate with the degree of hypothyroidism. A positive correlation was found between CK, CK-MB, LDH and SGOT/AST levels with TSH levels (r = +0.83, +0.73, +0.75, +0.67 respectively) and a negative correlation was found between CK, CK-MB, LDH & SGOT/AST levels with T3 (r = -0.51, -0.45, - 0.41, -0.38 respectively) and T4 levels (r = -0.77, - 0.68, -0.66, -0.65 respectively) [Table:2].

Discussion:

Hypothyroidism is a condition characterized by abnormally low thyroid hormone production. Hypothyroid patient have increase activity of serum creatine kinase that is mostly due to increase CK-MM as CK isoenzyme analysis in six cases of primary hypothyroidism showed only the MM isoenzyme to be present in four patients, and MM with a trace of MB in the other two[9]. This finding also confirms previous studies that indicated skeletal muscle to be the major source of the increase plasma CK activity [9,10] Hypothyroid patients have increased concentration of creatine kinase that is mostly due to increased CK-MM. However, CKMB has also been reported to increase above reference values in hypothyroid patients without apparent myocardial damage[11,12]. The study also found increase in LDH and AST/SGOT activity in patients with overt hypothyroidism. Fleisher GA et al also reported 37% of hypothyroid patients to have elevated LDH levels[13]. In another study elevation of LDH activity was found in 33% of patients with overt hypothyroidism and in 74% of patients with subclinical hypothyroidism and in a latter study 27 of 45 hypothyroid patients had elevated total LDH levels[14]. The levels of AST/SGOT were reported to be elevated in 60% of patients with hypothyroidism by Griffith PD [15]. Involvement of skeletal muscle is among the most prevalent clinical consequences of hypothyroidism. Histologically the muscle fibres show enlargement, focal myofibrillar degeneration, increase in central nuclei, glycogen accumulation and mitochondrial aggregations and type II fibre atrophy[16]. Slowed muscle contraction and relaxation, known as hypothyroid myopathy may be caused by a shift in the distribution of muscle fibre types from fasttwitch fibres to slow-twitch fibres. A reduction in muscle mitochondrial oxidative capacity and beta adrenergicreceptors, as well as the induction of an insulin-resistant state, may result in these changes. Evidence from a study by Sinclair and colleagues suggests that a decrease in muscle carnitine in patients with either hypothyroidism or hyperthyroidism may contribute to thyroid myopathy[17]. Muscle functions usually completely recover with thyroxine therapy[18,19,20]. The significant elevation of serum activities of these enzymes indicate muscle involvement in

hypothyroidism which may present as clinical or subclinical myopathy and needs high index of suspicion. These enzymes also correlate with disease severity and show a positive correlation with TSH levels and a negative correlation with T3and T4 levels.

Conclusion:

The significant elevation of serum CK, LDH & AST activities indicate muscle involvement in hypothyroidism and that these enzymes can be used as parameters for screening of hypothyroid patients.

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